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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,353	06/08/2007	Jay Lal Mehta	056291-5246	8786

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EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,353	MEHTA, JAY LAL	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19* is/are pending in the application.

4a) Of the above claim(s) *24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Remarks' filed on 30 October 2008 have been acknowledged and duly made of record.

Claim Rejections under 35 USC § 112, 1st paragraph are hereby withdrawn due to applicants' amendment to the claim.

The essence of applicants' argument with regard to the rejection under 35 USC § 103(a) has been considered.

Upon further consideration, the Qin et al. and the Leyland-Jones reference are also withdrawn.

However Robl '821 clearly teaches the classification of both agents as disclosed to be given in combination which would be obvious to try by the one of skill.

Further, the applicants' contain a limitation in claim 19 that could reasonably be interpreted broadly to include active agents in addition to candesartan and rosuvastatin, i.e., the limitation "*comprising*".

Thus, Robl '821 is proper due to the content of what it teaches and the obviousness in the well-known art to combine active agents of different classifications in order to treat the same disorder such as atherosclerosis in this case.

Robl '821 does not specifically teach the claimed invention. However, the reference does teach that these (2) compounds may be administered together for the treatment of arteriosclerosis.

Further, the applicants have the further burden to show that the combination treats atherosclerosis. However, the ratio as disclosed in the specification has a scope that is not commensurate with the disclosure in the instant claims.

All responses to the grounds of rejection have been sufficiently addressed and considered but are not found persuasive.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Robl (USPN 6,620, 821).

The incurrent and instant claim cites thus:

Claim 19 (currently amended): A method of treating or reducing the extent of atherosclerosis in a warm-blooded animal in need thereof, which comprises administering to said animal an effective amount of a combination comprising candesartan or a pharmaceutically acceptable salt thereof and rosuvastatin or a pharmaceutically acceptable salt thereof.

Robl teaches compounds of the following structure are HMG CoA reductase inhibitors and thus are active in inhibiting cholesterol biosynthesis, modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol, and **treating** hyperlipidemia, dyslipidemia, hormone replacement therapy, hypercholesterolemia, hypertriglyceridemia and **atherosclerosis** as well as Alzheimer's disease and osteoporosis.

With regard to an **effective amount of a combination comprising**, Robl teaches [a] preferred oral dosage form, such as tablets or capsules, will contain the ACE inhibitor or AII antagonist in an amount within the range from about 0.1 to about 500 mg, preferably from about 5 to about 200 mg and more preferably from about 10 to about 150 mg. Both candesartan and rosuvastatin taught in a combination formulation as disclosed above would preferably be in an amount of between

In the instant specification, applicants disclose an effective amount or suitable dosage as follows:

Suitable dosages of each component of the combination are those of the marketed commercial products. Alternatively, the synergy between the components may allow a lower dosage of one or both components to be used. For example, a dose of 4mg, 8 mg, 16 mg, 32 mg, or up to 160 mg of candesartan in combination with a dose of 80mg, 40mg, 20mg, 10 mg, 5 mg 2.5 mg of rosuvastatin may be used. It will be understood that any one of the doses of candesartan may be combined with any suitable dose of rosuvastatin.

In one aspect, 80mg of rosuvastatin is used. In another aspect, 40mg of rosuvastatin is used. In a further aspect, 20mg of rosuvastatin is used. In a further aspect, 10 mg of 20 rosuvastatin is used. In a further aspect, 5rag of rosuvastatin is used. In a further aspect, 2.5 mg of rosuvastatin is used.

In one aspect, between 32 and 160 mg, such as about 64 to 128 mg, for example 64 to 112 mg, such as about 64-96mg of candesartan is used. Conveniently, about 72mg of candesartan is used. In another aspect, 32 mg of candesartan is used. In a further aspect, 16 mg of candesartan is used. In a further aspect, 8 mg of candesartan is used. In a further aspect, 4 mg of candesartan is used.

(page 4, 4th - 6th paragraphs).

Thus, the suitable dosages disclosed in the Robl reference make the suitable dosages of claimed invention obvious.

Robl teaches candesartan (col 37, line 19).

Robl teaches rosuvastatin (col 28, line 21).

Robl teaches the embodiments drawn to combination therapy in the treatment of atherosclerosis.

The embodiment cites thus:

Thus, where desired, the compounds of structure I may be used in combination with one or more hypolipidemic agents or lipid-lowering agents, or lipid agents, or lipid modulating agents, and/or one or more other types of therapeutic agents including antidiabetic agents, anti-

obesity agents, antihypertensive agents, platelet aggregation inhibitors, anti-Alzheimer's agents, anti-dementia agents, anti-osteoporosis agents, and/or hormone replacement therapeutic agents, and/or other therapeutic agents, and/or other cardiovascular agents (including anti-anginal agents, anti-arrhythmic agents, anti-atherosclerosis agents, anti-inflammatory agents, anti-platelet agents, anti-heart failure agents), anti-cancer agents, anti-infective agents, hormone replacement agents, growth hormone secretagogues, selective androgen receptor modulators, and/or other therapeutic agents which may be administered orally in the same dosage form or in a separate oral dosage form, or by injection (col 28 , lines 33-49).

Further, in light of disclosure above, it would have been *prima facie* obvious to one of skill in the art to at once recognize a reasonable expectation of success directed to a method of treating atherosclerosis with combination therapy (candesartan and rosuvastatin) via the disclosure of Robl.

The scope and contents of the prior teaches a method of treating atherosclerosis with agents already art-known to reduce cholesterol. Combination therapy for hypercholesterolemia is also art-known. Candesartan and rosuvastatin have differing mechanisms of action as being part of two different and distinct classifications of drugs. Synergy is indicated as an obvious variant in the dual therapy treatments.

The differences in the prior art and the claims at issue is that candesartan is not taught in any direct combination with rosuvastatin. Instead the references discloses within such embodiments adequate suggestion, support, and direction toward combination therapy for atherosclerotic conditions.

Considering objective evidence present in the application indicating obviousness or nonobviousness, the instant claim cites limitations that clearly indicate obviousness. As said above, concomitant therapy with two or more drug agents in order to control atherosclerosis is an art-known protocol of therapy. It would be well within the purview of the one of skill to conduct routine experimentation with variable combinations of angiotensin II receptor antagonists (of which candesartan is a part) and HMG-CoA reductase inhibitor (of which rosuvastatin is a part). Accordingly, it would have been obvious to try based on the knowledge that these two agents treat atherosclerotic conditions via spectrum therapy, i.e., dual mechanisms of action on the human body to treat atherosclerosis.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shengjun Wang/
Primary Examiner, Art Unit 1617
TEB